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EXAMINER
NGUYEN, QUANG

ART UNIT	PAPER NUMBER
1632	13

DATE MAILED: 12/19/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Applicati n N .	Applicant(s)	
	09/445,604	ABATANGELO ET AL.	
	Examiner	Art Unit	
	Quang Nguyen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspond nc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 October 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) *87-121* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *87-121* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicant's amendment filed October 05, 2001 in Paper No. 12 has been entered. New claims 87-121 are pending in the present application, and they are examined on the merits herein.

The text of those sections of Title 35 U.S.C. Code not included in this action can be found in a prior office action.

Claim Rejections - 35 USC § 102

New claims 87, 90, 91, 93, 94, 99, 103-105, 107-109, 112, 113, 115, 116 and 121 are rejected under 35 U.S.C. 102(b) as being anticipated by Bellini et al. (WO 96/37519 with a published date of 28 November 1996; IDS) for the same reasons already set forth in the previous Office Action.

Claims 87, 90-91, 93-94, 99, 103-105 and 107-108 are drawn to a biological material comprising: a) at least one autologous or homologous cellular line selected from the group consisting of endothelial cells, glandular cells, skin adnexa and germinative cells of hair bulbs; and b) a biocompatible three-dimensional matrix, on which said cellular line is seeded and grown, said matrix comprising at least a hyaluronic acid derivative selected from the group recited in claim 87.

Claims 109, 112-113, 115-116 and 121 are drawn an in vitro biological material comprising: a) at least one cellular line selected from the group consisting of endothelial cells, glandular cells, skin adnexa and germinative cells of hair bulbs; and b) a biocompatible three-dimensional matrix, on which said cellular line is seeded and

grown, said matrix comprising at least a hyaluronic acid derivative selected from the group recited in claim 109.

It should be noted that for composition claims, the intended use is not given any patentable weight in view of the prior art.

Bellini et al. teach a polysaccharide hydrogel material consisting of a crosslinked product of a functionalized derivative of alginic acid or hyaluronic acid, whose carboxylic groups are partially esterified (preferably 75% of the carboxylic groups) with an unsaturated aliphatic or an araliphatic alcohol, and the remaining carboxylic groups are partially salified with a cation selected from the group consisting of alkaline, alkaline earth metal cation or with tetraalkylammonium (page 2, first paragraph and page 4, lines 21-26). Additionally Bellini et al. teach that the hydrogel material can be prepared in the form of fibers, films, membranes, threads, gauzes and sponges, which are three dimensional objects or matrix (page 2, lines 16 and page 6, lines 1-10). Moreover, Bellini et al. teach that the hydrogel material can be used as supports of human cells such as keratinocytes, fibroblasts, osteocytes, chondrocytes, urocytes, stem cells, endothelial cells, Kupfer's and Langerhan's cells (page 6, lines 11-14). It should be noted that the endothelial cells, Kupfer's and Langerhan's cells growing on the hydrogel material support of Bellini et al. are indistinguishable from autologous endothelial and glandular cell lines claimed by Applicants. With respect to claim 90, it is well known that endothelial cells are isolated from tissues having blood vessels.

Accordingly, Bellini et al. teachings meet all limitations recited in the claims, and thus Bellini et al. anticipate the instantly claimed invention.

Response to Arguments

Applicants' arguments related to the above rejection in the Amendment filed on October 05, 2001 in Paper No. 12 (pages 13-14) have been fully considered.

Applicants argued that "In Bellini, the hydrogel material is a derivative of a hyaluronic acid ester, not a three-dimensional hyaluronic acid ester such as that claimed in the present invention". Applicants further argued that in Bellini, the polymer has a molecular weight higher than the precursor hyaluronic acid ester having ethylenic unsaturation due to a radical polymerization by UV, β and γ radiations. Therefore, products having a different molecular weight show different physical-chemical properties. Applicants further noted that the polysaccharide hydrogel material of Bellini has a different physical structure from the hyaluronic acid derivative-based support of the presently claimed invention by being a compact three dimensional (wall to wall) structure allowing a greater mechanical resistance. Examiner respectfully finds Applicants' arguments to be unpersuasive for the following reasons.

The biological material of the presently claimed invention comprises a biocompatible three-dimensional matrix which comprises a hyaluronic acid derivative selected from the group recited in the claims. Applicants' argument regarding to a three-dimensional hyaluronic acid ester is not germaine to the claimed invention. Moreover, a hyaluronic acid ester is not a three-dimensional structure. Bellini clearly teaches that the hydrogel material can be prepared in the form of fibers, films, membranes, threads, gauzes and sponges, which are three dimensional objects or

matrix (page 2, lines 16 and page 6, lines 1-10). The polysaccharide hydrogel material of Bellini contained a cross-linked product of a functionalized derivative of alginic acid or hyaluronic acid, whose carboxylic are partially esterified (preferably 75% of the carboxylic groups) with an unsaturated aliphatic or an araliphatic alcohol, and the remaining carboxylic groups are partially salified with a cation selected from the group consisting of alkaline, alkaline earth metal cation or with tetraalkylammonium (page 2, first paragraph and page 4, lines 21-26). Thus, it is apparent that the polysaccharide hydrogel material of Bellini is a species encompassed within the broad scope of a biological material of the instantly claimed invention.

Although the polysaccharide hydrogel material of Bellini differs chemically and physically from the hyaluronic acid derivative-based three-dimensional matrix of the biological material of the present invention, the instant claims embrace a species taught by Bellini. There is no recitation of any physical or chemical properties for the three-dimensional matrix of the biological material of the present invention that distinguish it from the polysaccharide hydrogel material of Bellini.

Accordingly, claims 87, 90, 91, 93, 94, 99, 103-105, 107-109, 112, 113, 115, 116 and 121 remain rejected for the reasons set forth above.

Claim Rejections - 35 USC § 103

Claims 87, 94-95, 109, 116-117 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bellini et al. (WO 96/37519) in view of Cialdi et al.(U.S. Patent

6,027,741; Cited previously) for the same reasons set forth in the previous Office Action.

Claims 87 and 94-95 are drawn to a biological material comprising: a) at least one autologous or homologous cellular line selected from the group consisting of endothelial cells, glandular cells, skin adnexa and germinative cells of hair bulbs; and b) a biocompatible three-dimensional matrix, on which said cellular line is seeded and grown, said matrix comprising at least a hyaluronic acid derivative selected from the group recited in claim 87; the same wherein component b) is in the form of a nonwoven fabric..

Claims 109 and 116-117 are drawn an in vitro biological material comprising: a) at least one cellular line selected from the group consisting of endothelial cells, glandular cells, skin adnexa and germinative cells of hair bulbs; and b) a biocompatible three-dimensional matrix, on which said cellular line is seeded and grown, said matrix comprising at least a hyaluronic acid derivative selected from the group recited in claim 109; the same wherein component b) is in the form of a nonwoven fabric.

Bellini et al. teach a polysaccharide hydrogel material consisting of a crosslinked product of a functionalized derivative of alginic acid or hyaluronic acid, whose carboxylic groups are partially esterified (preferably 75% of the carboxylic groups) with an unsaturated aliphatic or an araliphatic alcohol, and the remaining carboxylic groups are partially salified with a cation selected from the group consisting of alkaline, alkaline earth metal cation or with tetraalkylammonium (page 2, first paragraph and page 4, lines 21-26). Additionally Bellini et al. teach that the hydrogel material can be prepared in the

form of fibers, films, membranes, threads, gauzes and sponges, which are three dimensional objects or matrix (page 2, lines 16 and page 6, lines 1-10). Moreover, Bellini et al. teach that the hydrogel material can be used as supports of human cells such as keratinocytes, fibroblasts, osteocytes, chondrocytes, urocytes, stem cells, endothelial cells, Kupfer's and Langerhan's cells (page 6, lines 11-14). It should be noted that the endothelial cells, Kupfer's and Langerhan's cells growing on the hydrogel material support of Bellini et al. are indistinguishable from autologous endothelial and glandular cell lines claimed by Applicants. Bellini et al. do not teach that the hydrogel material can be prepared in the form of a nonwoven fabric or the use of sulfated hyaluronic acid to support the aforementioned human cells.

Cialdi et al. disclose that sulfated hyaluronic acid, hyaluronate esters and salts thereof can be used to prepare biomaterials in various forms such as gauzes, threads, gels, hydrogels, sponges, membranes, non-woven tissues and microspheres, all of which are three dimensional objects or matrix (See abstract and column 14, lines 53-60). Furthermore, Cialdi et al. teach that human umbiblical vein endothelial cells proliferate and exhibit better growth in culture medium containing sulfated hyaluronic acid than cells cultured in the medium containing hyaluronic acid or control medium (See example 16, columns 14 and 15).

Accordingly, at the time of the instant invention it would have been obvious to an ordinary skilled artisan to use sulfated hyaluronic acid in any of the form of gauzes, threads, gels, hydrogels, sponges, non-woven tissues, microspheres as supports for endothelial cells, Kupfer's and Langerhan's cells because Bellini et al. already teach

that polysaccharide hydrogel materials composing of crosslinked products of functionalized derivatives of hyaluronic acids can be used as supports for such cells. One of ordinary skilled in the art would have been motivated to use supports made up of sulfated hyaluronic acid disclosed by Cialdi et al., because Cialdi et al. already demonstrate in tissue culture that at least for endothelial cells, sulfated hyaluronic acid promotes the proliferation of endothelial cells. Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Response to Arguments

Applicants' arguments related to the above rejection in the Amendment filed on October 05, 2001 in Paper No. 12 (pages 14-17) have been fully considered.

Applicants argued that with respect to the Bellini reference, Bellini discloses: "a different hyaluronic acid derivative from those contemplated in the present invention with better properties in term of compactness than those of some hyaluronic acid derivatives disclosed in the present, and envisaging among the possible uses of said different hyaluronic acid derivative, the use as support for a plethora of cells and among them also of some cells contemplated in the biological materials as presently claimed, however not giving any experimental evidence for such a use". With respect to the combination with the Cialdi reference, Applicants argued that "disclosing sulfated hyaluronic acid derivatives, namely the hyaluronic acid derivative of class (C) encompassed in the instant invention, also in the form of a three dimensional material-teaching that HUVEC cells grow and proliferate in a medium containing a sulfated

hyaluronic acid, but silent about use of said material as support for said type of cells or other weak and fragile cells." Additionally, Cialdi does not teach HUVEC and other weak and fragile cells when seeded on said materials in the form of a three dimensional matrix survive longer than when seeded on plastic dishes. Examiner respectfully finds Applicants' arguments to be unpersuasive for the following reasons.

With respect to the Bellini reference, although Bellini discloses a different hyaluronic acid derivative from those contemplated in the present invention, the instant claims embrace a biological material species of Bellini for the reasons already stated in the response to the rejection of claims 87, 90, 91, 93, 94, 99, 103-105, 107-109, 112, 113, 115, 116 and 121 above. It is unclear from Applicants' arguments why the polysaccharide hydrogel material of Bellini would not be able to support the growth of endothelial cells, Kupfer's and Langerhan's cells as asserted by Bellini, particularly the biological material of Bellini has physical properties decidedly better than those of some hyaluronic acid derivatives contained in the support of the biological material of the present invention as acknowledged by Applicants (see page 15, first three lines of the fourth full paragraph). Moreover, the polysaccharide hydrogel material of Bellini comprises the same starting material in the making of a biocompatible three-dimensional matrix, which is a functionalized hyaluronic acid whose carboxylic groups are partially esterified with an unsaturated aliphatic or an araliphatic alcohol, as that for the presently claimed biological material. With respect to the Cialdi reference, although Cialdi is silent about the specific use of sulfated hyaluronic acid in any of the form of gauzes, threads, gels, hydrogels, sponges, non-woven tissue, micropheres

encompassed by the present claimed invention as a support for endothelial cells, one of ordinary skilled artisan would have been motivated to do so because in the presence of sulfated hyaluronic acid as shown in cell cultures, endothelial cells exhibit a better growth and at least sulfated hyaluronic acid is not toxic to endothelial cells. Furthermore, Bellini already taught that a polysaccharide hydrogel material in the form of fibers, films, gauzes and sponges comprising crosslinked product of a functionalized derivative of hyaluronic acid can be used as a support for human endothelial cells, Kupfer's and Langerhan's cells. Applicants have not provided any objective evidence why it would not be an advantage for using sulfated hyaluronic acid as a support for endothelial cells? With respect to the issue that Cialdi does not teach about the survival times of HUVEC in the medium containing sulfated hyaluronic acid, it is irrelevant. In light of the teachings of Bellini and Cialdi, one of ordinary skilled artisan can just be motivated to use the sulfated hyaluronic acid disclosed by Cialdi as a support for a better proliferation and growth of endothelial cells. Furthermore, the claims do not recite any limitation concerning the survival of seeded cells.

Accordingly, claims 87, 94-95, 109, 116-117 remain rejected for the reasons set forth above.

Claims 98 and 120 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bellini et al. (WO 96/37519) for the same reasons set forth in the previous Office Action.

Claims 98 and 120 are drawn to a process for the preparation of the biological material according to claim 88 and 110, respectively.

Bellini et al. teach a polysaccharide hydrogel material consisting of a crosslinked product of a functionalized derivative of alginic acid or hyaluronic acid, whose carboxylic groups are partially esterified (preferably 75% of the carboxylic groups) with an unsaturated aliphatic or an araliphatic alcohol, and the remaining carboxylic groups are partially salified with a cation selected from the group consisting of alkaline, alkaline earth metal cation or with tetraalkylammonium (page 2, first paragraph and page 4, lines 21-26). Additionally Bellini et al. teach that the hydrogel material can be prepared in the form of fibers, films, membranes, threads, gauzes and sponges, which are three dimensional objects or matrix (page 2, lines 16 and page 6, lines 1-10). Moreover, Bellini et al. also teach that the hydrogel material can be used as supports of human cells such as keratinocytes, fibroblasts, osteocytes, chondrocytes, urocytes, stem cells, endothelial cells, Kupfer's and Langerhan's cells (page 6, lines 11-14). It should be noted that the endothelial cells, Kupfer's and Langerhan's cells growing on the hydrogel material support of Bellini et al. are indistinguishable from autologous endothelial and glandular cell lines claimed by Applicants. Bellini et al. do not teach explicitly the process of making the hydrogel material supports containing the aforementioned cells. However, at the effective filing date of the present application, the isolation of these cells and the seeding of these cells in the polysaccharide hydrogel materials of Bellini et al. are evident by the references supplied in the IDS. Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

It is noted that Applicants did not address this rejection in the Amendment filed on October 05, 2001 in Paper No. 12.

Following is a new ground of rejection necessitated by Applicants' amendment.

Claim Rejections - 35 USC § 112

Claims are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a biological material comprising: a) cells selected from the group consisting of endothelial cells, glandular cells, skin adnexa and germinative cells of hair bulbs, and b) a bio compatible three-dimensional matrix, on which said cells are seeded and grown, said matrix comprising a hyaluronic acid derivative selected from the recited group in claim 87 or claim 109; a process for preparing the same and a method for carrying out human and veterninary surgery utilizing the same, does not reasonably provide enablement for other embodiments of the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 87-89, 91-97, 99-105, 107-108 are drawn to a biological material comprising: a) at least one autologous or homologous cellular line selected from the group consisting of endothelial cells, glandular cells, skin adnexa and germinative cells of hair bulbs; and b) a biocompatible three-dimensional matrix, on which said cellular

line is seeded and grown, said matrix comprising at least a hyaluronic acid derivative selected from the group recited in claim 87; a process for preparing the same biological material and a method for carrying out human and veterinary surgery utilizing the same biological material.

Claims 109-111, 113-121 are drawn an *in vitro* biological material comprising: a) at least one cellular line selected from the group consisting of endothelial cells, glandular cells, skin adnexa and germinative cells of hair bulbs; and b) a biocompatible three-dimensional matrix, on which said cellular line is seeded and grown, said matrix comprising at least a hyaluronic acid derivative selected from the group recited in claim 109; a process for preparing the same biological material.

The specification teaches by exemplification the isolation and culture conditions in the presence of a three-dimensional structure such as a non-woven HYAFF. The biological material of the present invention comprises a biocompatible three-dimensional matrix comprising a hyaluronic acid derivative with various cell types, including HUVEC, isolated liver cells, isolated islets of Langerhans and isolated skin adnexa. The specification discloses that fragile cells such as endothelial cells, glandular cells and skin adnexa, germinative cells of hair bulbs and others can efficiently grow on a hyaluronic acid derived matrix. Furthermore, the specification discloses optimal culture conditions for the growth of these cells in the hyaluronic acid derived matrix, such as in the presence of a medium treated with fibroblasts or in a co-culture with fibroblasts seeded on the matrix at different time periods. The above evidence has been noted and considered. However, the evidence can not be

reasonably extrapolated to the instant broadly claimed invention for the reasons discussed below.

The instant claims encompass a biological material comprising at least one cellular line selected from a group consisting of endothelial cells, glandular cells, skin adnexa and germinative cells of hair bulbs as well as methods for making and using the same. As is well known in the art, a characteristic of a cell line is its ability to divide indefinitely in cultures, and therefore providing an unlimited source of cells of a standardized, genetically homogenous type (See attached pages 892-893 in Molecular Biology of the Cell, Third Edition, Alberts et al., Eds., 1994). Apart from the well characterized HUVEC line known in the art, at the effective filing date of the present application, cell lines derived from glandular cells, skin adnexa and germinative cells of hair bulbs encompassed by the scope of the instant claims are not available. Nor does the instant specification provide any guidance for one skilled in the art on how to make and use such cell lines. Furthermore, it is also unclear whether the cell lines contemplated by Applicants can still retain the cellular characteristics of glandular cells, skin adnexa and hair bulbs, apart from their immortality. The physiological art is recognized as unpredictable (MPEP 2164.03). As set forth in *In re Fisher*, 166 USPQ 18 (CCPA 1970), compliance with 35 USC 112, first paragraph requires:

> That scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the are; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved.

Accordingly, due to the lack of sufficient guidance provided by the specification, the unpredictability of the physiological art, and the breadth of the claims, it would have required undue experimentation for one skilled in the art to make and use the biological material and methods of making and using the same as claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 87-108 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 87 and its dependent claims, it is unclear what is encompassed by the phrase "homologous cellular line". The cellular line is homologous to what? What is homologous in the cellular line? Since the phrase is not defined in the specification, the metes and bounds of the claims can not be clearly determined. Clarification is requested. Similarly, it is unclear what is encompassed by the phrases "homologous fibroblasts" and "homologous endothelial cells" in claims 98 and 101, respectively for the same reasons.

In claim 106, as written it is unclear what exact do Applicants intend to claim. It appears that the claim is incomplete, without any recitation of the steps involved in the claimed method. It is also unclear what is the relationship between the biological material of claim 104 in the claimed method. The metes and bounds of the claim can not be clearly determined.

Claim Rejections - 35 USC § 102

Claim 99 is rejected under 35 U.S.C. 102(b) as being anticipated by Bellini et al. (WO 96/37519).

The claim is drawn to a method of carrying out human and veterinary surgery which comprises employing in said surgery the biological material as defined in claim 87.

Bellini et al. teach a polysaccharide hydrogel material consisting of a crosslinked product of a functionalized derivative of alginic acid or hyaluronic acid, whose carboxylic groups are partially esterified (preferably 75% of the carboxylic groups) with an unsaturated aliphatic or an araliphatic alcohol, and the remaining carboxylic groups are partially salified with a cation selected from the group consisting of alkaline, alkaline earth metal cation or with tetraalkylammonium (page 2, first paragraph and page 4, lines 21-26). Additionally Bellini et al. teach that the hydrogel material can be prepared in the form of fibers, films, membranes, threads, gauzes and sponges, which are three dimensional objects or matrix (page 2, lines 16 and page 6, lines 1-10). Moreover, Bellini et al. teach that the hydrogel material can be used as supports of human cells such as keratinocytes, fibroblasts, osteocytes, chondrocytes, urocytes, stem cells, endothelial cells, Kupfer's and Langerhan's cells (page 6, lines 11-14). It should be noted that the endothelial cells, Kupfer's and Langerhan's cells growing on the hydrogel material support of Bellini et al. are indistinguishable from autologous endothelial and glandular cell lines claimed by Applicants. Bellini et al. further teach that their

polysaccharide hydrogel material can be utilized in numerous fields, from cosmetics to surgery and medicine, particularly as tissue substitutes and as agents to enbale the adhesion of tissue surfaces (pages 5-6).

Accordingly, Bellini et al. anticipate the instant claim.

Conclusions

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136 (a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (703) 308-8339.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, Dave Nguyen, may be reached at (703) 305-2024, or SPE, Karen Hauda, at (703) 305-6608.

Any inquiry of a general nature or relating to the status of this application should be directed to Patent Analyst, Patsy Zimmerman, whose telephone number is (703) 308-0196.

Quang Nguyen, Ph.D.

DAVE T. NGUYEN
PRIMARY EXAMINER